REMARKS

The following remarks are in response to the Examiner's Office Action mailed on April 15, 2004. Claims 1-17 are pending.

Claims 1-17 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Kain et al. (U.S. Patent No. 6,306,600) in view of Anderson et al. (U.S. Patent No. 6,546,249).

Independent claims 1, 3, 6, 8, and 9 specify a method for selecting cells based on whether the cells express a short-lived protein. Each of the claimed methods is a high throughput assay for screening a library of cells within which a library of different fusion proteins is expressed. According to the method, the library of different fusion proteins are expressed first and then allowed to degrade in the cells. As specified in claim 1, the cells expressing short-lived proteins are selected and exposed to various agents/conditions such that the agent(s)/condition(s) affecting degradation of the fusion proteins are selected.

In contrast, Kain et al. merely teaches a method of inhibiting further expression of a single fusion protein, e.g., EGFP-MODC, in cells. *See* Abstract. As acknowledged by the Examiner, Kain et al. does not teach a method for selecting cells expressing short-lived proteins by utilizing cells expressing a library of different fusion proteins.

Anderson et al. fails to teach or suggest the claimed methods of utilizing cells expressing a library of different fusion proteins to screen for **agents that are contacted with the cells and affect degradation of the different fusion proteins**. Specifically, Anderson et al. discloses the use of scaffold proteins, particularly green fluorescent protein (GFP), in **fusion constructs with random and defined peptides and peptide libraries. These peptides in the constructs are screened** for their ability to confer a particular phenotype to a cell, such as the ability to increase the cellular expression levels, to decrease the cellular catabolism, to increase the conformational stability relative to linear peptides, and to increase the steady state concentrations of the random peptides and random peptide library members expressed in cells for the purpose of detecting the presence of the peptides and screening random peptide libraries. *See* Abstract. Thus, this reference teaches screening for agents that are **covalently linked to a scaffold protein** through co-expression of the nucleotides encoding the peptide and the scaffold protein. See "Summary of the Invention", column 2, lines 8-

17. Therefore, Anderson et al. fails to supplement the claim elements missing from Kain et al. that are required for the establishment a prima facie case of obviousness under 35 U.S.C. §103(a).

To establish a prima facie case of obviousness, the Examiner bears the burden of proving 1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; 2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention; and 3) one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success of the claimed invention. *In re Vaeck*, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re O'Farrell*, 853 F. 2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); and *In re Dow Chem.*, 837 F. 2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Neither Kain et al. nor Anderson et al. contains a suggestion or motivation to combine these two references in such a way as to achieve the claimed invention. As discussed above, none of the cited references teaches or suggests the claimed methods of utilizing cells expressing a library of different fusion proteins to screen for agents that are contacted with the cells and affect degradation of the different fusion proteins. Kain et al. focuses on the studies of degradation of a single fusion protein, e.g., EGFP-MODC and does not give a clue as to whether or why a library of different fusion proteins should be expressed and agents should be screened for their effects on degradation of the fusion proteins after the agents are contacted with the cells expressing the fusion proteins.

On the other hand, Anderson et al. desired to find peptide(s) that confer(s) a scaffold protein an improved property, such as enhanced conformational stability. *See* Abstract. To achieve this goal, random peptide libraries are linked to the scaffold protein to form fusion protein libraries, and cells expressing the peptide-scaffold fusion proteins with the altered phenotype are selected. "The presence of the fusion protein is verified to ensure that the peptide was expressed and thus the altered phenotype can be due to the presence of the peptide." Column 47, lines 41-45. Thus, contacting the cells expressing the random peptide fusion proteins with agents that modulate protein degradation would defeat Anderson et al.'s purposes of finding the desirable peptide because the correlation of the peptide with the phenotype of the cells is destroyed by the interference of the agents. Therefore, the combination of Kain et al. and Anderson et al. fails to motivate one of ordinary skill in the art to modify either one of the references to arrive at the present invention.

In view of the failure of the cited reference to teach or suggest the claimed invention, a prima facie case of obviousness under 35 U.S.C. §103(a) has not been established. Withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

In light of the amendments and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent to issuance. Should the Examiner have any questions, Examiner is encouraged to telephone the undersigned.

Respectfully,
WILSON SONSINI GOODRICH & ROSATI

Date: August 13, 2004 By: 

Shirley Chen, Ph.D.
Reg. No. 44,608

650 Page Mill Road
Palo Alto, CA 94304-1505
Direct dial: (650) 565-3856
Customer No. 021971